Applicant acknowledges and thanks the Examiner for withdrawal of the rejection of claims 1-8 under 35 U.S.C. § 112, second paragraph.

Based on the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Description of the Invention

The present invention relates to methods of identifying binding sites on proteins, methods for identifying classes of compounds suitable for binding a protein, and methods of conducting experiments to identify compounds that interact with a protein to affect a biological process.

Drawings

Applicant wishes to defer submission of a petition for acceptance of photographs or color photographs.

Claim Rejections Under 35 U.S.C. § 102

The Examiner has rejected claims 1-8, 11, 13 and 14 under 35 U.S.C. § 102(b) as being anticipated by Resat, H. *et al.*, *Biophys. J. 71*:1179-1190 (1996) ("Resat"). See page 3 of the Office Action. Applicant traverses this rejection.

The Examiner states at page 3 of the Office Action that Resat teaches a method for determining likely locations for solvating waters in a dCpG/proflavine crystal hydrate using Monte Carlo simulation studies. The Examiner states that the mobility of atoms are estimated from B factors.

Resat does not anticipate the claimed invention. Resat does not conduct a simulating annealing of chemical potential calculation at separate values of B. The "B factor" discussed in Resat is not the same as the B *parameter* in the captioned application. The B factor in Resat is a temperature factor from which the mobility of atoms in crystal structures may be estimated (p. 1179, col. 1 of Resat), while the B parameter in the captioned application is a measure of chemical potential.

Page 1182 of Resat discusses the B parameter, but states that the B parameter (not B factor) is fine tuned before the calculation, but then kept constant during the data acquisition. Thus, a simulated annealing of chemical potential calculation at separate values of B is not conducted in Resat. Therefore, Resat does not anticipate the claims of the captioned application. Applicant respectfully requests the Examiner to reconsider and withdraw the rejection over Resat.

Claim Rejections Under 35 U.S.C. § 103

The Examiner has rejected claim 11 under 35 U.S.C. 102(a) as being unpatentable over Resat in view of Morgantini, *J Am Chem Soc* 1995, 117(22), 6057-63 or Calafat, *J Am Chem Soc* 1997, 119(16), 3656-3664 or Blasko, *Journal of Organic Chemistry*, 10/8/93, Vol. 58, No. 21, pages 5738-5747 or Siepmann, *Molecular Physics* 1993, Vol. 79, no. 3, 457-473 or Koone, *Journal of Physical Chemistry*, 16 NOV 1995, vol. 99, No. 46, pages 16976-16981 or Gibson, *Journal of Physical Chemistry*, 16 MAR 1995, Vol. 99, No. 11, pages 3765-3773 or Brandmeier, *Helv. Chim. Acta*, 1994, 77(1), pages 70-85 or Johnson, *Inst. Phys. Conf. Ser.*, 1991, 114 or Reson, Ioniz Spectrosc. 1990, 145-50 or Basson, J. Phys. D: Appl. Phys. 1988, 21(9), pages

1434-7 or Ranineri, *Chemical Physics* 183, 1994, 187-205 or Mokrosz, *Journal of Heterocyclic Chemistry*, JUL/AUG 1996, Vol. 33, No. 4, pages 1207-1210 or Duggan, *Journal of Medicinal Chemistry*, 27 SEP 1996, Vol. 39, No. 20, pages 4007-4016 or Clough, Macromolecules, 15 FEB 1993, Vo. 26, No. 4, pages 597-600 or Lunazzi, Journal of Organic Chemistry, 1997, 62/7 (2263-2266) or Lee, *Journal of the American Chemical Society*, 1996, 118/3, 502-508. See page 4 of the Office Action.

Applicant believes that the Examiner intended to refer to claim 12. Accordingly, the following remarks are directed to claim 12, and not to claim 11. Applicant traverses this rejection.

At page 6 of the Office Action the Examiner states:

> It would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the molecular dynamic studies with water as the organic fragment as per the teachings of Resat and to further perform the method with any of acetone, aldehyde, amide, ammonia, benzene, carboxylic acid, 1,4-diazine, ester, ether, formaldehyde, furan, imidazole, methane, methanol, phospho-acid, pyridine, pyrimidine, pyrrole, thiol, or thiophene as the organic fragment because teachings of Morgantini, Calafat, Blasko, Siepmann, Koone, Gibson, Brandmeier, Johnson, Basson, Raineri, Mokrosz, Duggan, Clough, Lunazzi and/or Lee as cited above collectively demonstrate the utility of applying molecular dynamic studies to any of the compounds and analyzing binding to biomolecules.

Applicant respectfully disagrees. None of the references cited above cure the deficiencies of Resat. Morgantini, Calafat, Blasko, Siepmann, Koone, Gibson, Brandmeier, Johnson, Basson, Raineri, Mokrosz, Duggan, Clough, Lunazzi or Lee do not teach conducting, at separate values of parameter B, two or more simulated annealing of chemical potential calculations. Therefore, one of ordinary skill in the art would not have been motivated to perform these calculations with a reasonable expectation of success.

The Federal Circuit has stated that for a successful 35 U.S.C. § 103 rejection, it is necessary to show both the motivation to combine the applied art and a reasonable expectation of success of obtaining the claimed invention from the combination of the art. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Further, there must be some objective teaching in the art which would lead one of skill in the art to combine the relevant teachings of the references. *In re Fine*, 2 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). If either prong of *Vaeck* (*i.e.*, motivation or expectation of success), and the Examiner cannot show both motivation to combine the applied art and a reasonable expectation of success, the Examiner has not made out a *prima facie* case of obviousness and the rejection of claim 12 is incorrect.

There is nothing in Resat that would lead to its combination with Morgantini, Calafat, Blasko, Siepmann, Koone, Gibson, Brandmeier, Johnson, Basson, Raineri, Mokrosz, Duggan, Clough, Lunazzi or Lee. However, even if the cited references were taken together in any combination, they do not make obvious a method of identifying binding sites on a macromolecule by conducting, at separate values of parameter B, two or more simulated annealing of chemical potential calculations using the ORF as the inserted solvent.

Further, claim 3 requires conducting two or more simulated annealing of chemical potential calculations for each of two or more ORFs to identify clusters where two or more distinct ORFs bind. There is nothing in Resat or Morgantini, Calafat, Blasko, Siepmann, Koone, Gibson, Brandmeier, Johnson, Basson, Raineri, Mokrosz, Duggan, Clough, Lunazzi or Lee which would lead one of skill in the art to combine Resat with at least two of the cited references in order to practice claim 3. Applicant respectfully requests the Examiner reconsider and withdraw the rejection over Resat in combination with Morgantini, Calafat, Blasko, Siepmann,

Koone, Gibson, Brandmeier, Johnson, Basson, Raineri, Mokrosz, Duggan, Clough, Lunazzi or Lee.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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